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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/993,669	11/27/2001	Ann-Kristin Karlsson	06275-160002	1605

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EXAMINER	
MAIER, LEIGH C	
ART UNIT	**PAPER NUMBER**
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/993,669	KARLSSON ET AL.	
	Examiner	Art Unit	
	Leigh C. Maier	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *65,66,68-144 and 147-157* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *65,66,68-144 and 147-157* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/26/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 26, 2006 has been entered.

Claims 65, 84, 104, 146 and 147 have been amended. Claims 148-157 are newly added. Claims 65, 66, 68-144 and 147-157 are pending. Any rejection or objection not expressly repeated has been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Applicant's arguments with respect to the amended claims have been considered but are moot in view of the new grounds of rejection.

Claim Rejections - 35 USC § 112 – 2nd paragraph

Claims 94-114 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 94-100 are drawn to a "suspension *consisting of* [a budesonide product] suspended in an aqueous solution." (emphasis added) However, these claims are further limited by claims 101-114 that use "comprising" language. Because the claims use a combination of "closed" (consisting of) and "open" (comprising) language, it is not clear what, if anything, is

meant to be excluded. Therefore, one of ordinary skill would not be apprised of the metes and bounds of the claims.

Claim Rejections - 35 USC § 103

Claims 65, 66, 68-83, 94-97, 101-109, 112, 115-117, 124-126, 130-132 and 139-141 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harris et al (US 6,187,765) in view of Jakupovic et al (WO 96/32095).

Harris teaches the preparation of a composition of a glucocorticosteroid, mometasone furoate (MF), in the form of a sterile, aqueous suspension comprising a nonionic surfactant, a buffer and soluble salt. See examples 3, 5 and 6. The reference notes the importance of sterility in compositions to be inhaled. The product is prepared using a process that comprises pumping a solution of MF through a sterilizing filter, followed by precipitating with water, suspending and micronizing to a preferred particle size of less than 2.0 μm. The reference further discusses the use of particles having a range of 0.5-5 μm. See col 1, lines 27-42; col 2, beginning at line 65 and continuing through col 3, line 17; and examples 1 and 2. The reference further teaches that this product is useful for the treatment of airway disorders including asthma and various inflammatory conditions. See col 1, lines 17-25. The reference clearly draws equivalence between MF and other glucocorticosteroids, such as budesonide and beclomethasone. See col 2, lines 5-15. The reference teaches that budesonide is known to be used as a suspension comprising a citrate buffer and a surfactant. The reference does not teach a sterile suspension comprising micronized budesonide.

Jakupovic teaches respirable particles of budesonide, produced by using water to precipitate the budesonide from an organic solution. See abstract and examples. The reference further suggests the preparation of other glucocorticosteroid, such as mometasone, beclomethasone and fluticasone. See page 4, lines 27-29. The product is for nasal inhalation with a particle range of about 0.1 μm to about 10 μm. See paragraph bridging pages 3 and 4. A product wherein 90% of the particles have a diameter of less than 5.7 μm is exemplified. See example 1, page 8 and page 4, lines 4-6. The reference further teaches the preparation of pharmaceutical compositions by adding any of a variety of pharmaceutically acceptable carriers. See page 5, beginning line 11, continuing through page 6, line 17.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare a sterile suspension comprising micronized budesonide for the treatment of inflammatory conditions and asthma using the method of Harris. One of ordinary skill would reasonably expect success in using the Harris method for the preparation of sterile, micronized budesonide. Although the Harris process exemplifies mometasone, it would be within the scope of the artisan to select an appropriate solvent and precipitation conditions for budesonide through routine experimentation. It is known from Jakupovic that budesonide may be precipitated from a solution of methanol with water. Both references draw equivalence between mometasone and budesonide. In the absence of unexpected results, it would be further obvious to select appropriate additives and optimize their concentrations, as well as the size of the micronized particles through routine experimentation. Regarding pH, Harris suggests the use of a pH range of 3 to 7 using a citrate buffer for mometasone and teaches that budesonide is sold in a

suspension comprising a citrate buffer. Therefore, one of ordinary skill would reasonably expect a similar appropriate pH range for budesonide and optimize accordingly.

Claims 110 and 111 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harris et al (US 6,187,765) in view of Jakupovic et al (WO 96/32095) as applied to claims 65, 66, 68-83, 94-97, 101-109, 112, 115-117, 124-126, 130-132 and 139-141 above, and further in view of Guy et al (US 5,540,930).

Harris and Jakupovic teach as set forth above. The references do not teach the use of EDTA.

Guy teaches that EDTA—alone or in combination with benzalkonium chloride—has utility in preventing microbial contamination of glucocorticosteroid suspensions. See col 3, lines 35-40; col 4, lines 1-14; and col 5, lines 1-5.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare a sterile suspension comprising budesonide as set forth above. It would be further obvious to prepare one comprising EDTA for its utility as an antimicrobial to protect the sterile composition from microbial contamination.

Claims 113, 114, 121-123, 127-129, 136-138 and 142-144 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harris et al (US 6,187,765) in view of Jakupovic et al (WO 96/32095) as applied to claims 65, 66, 68-83, 94-97, 101-109, 112, 115-117, 124-126, 130-132 and 139-141 above, and further in view of Helzner et al (WO 97/01341).

Harris and Jakupovic teach as set forth above. The references do not teach the use of thickeners or the treatment of allergic conditions or rhinitis.

Helzner teaches that anti-inflammatory glucocorticosteroids, such as budesonide and beclomethasone. See paragraph bridging pages 1 and 2. The reference teaches a variety of typical pharmaceutical additives, such as antimicrobials, buffers, surfactants and viscosity builders (thickeners). The reference teaches a preferred pH range of about 4.0 to 6.5. See paragraph bridging pages 7 and 8 and the general formula directly thereafter.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare a sterile suspension comprising micronized budesonide, as discussed above. It would be further obvious to administer this product for the treatment of allergic rhinitis with a reasonable expectation of success because Helzner had taught that budesonide has this utility. It would be further within the scope of the artisan to select appropriate additives, such as thickeners, and determine the appropriate concentration through routine experimentation.

Claims 118-120 and 133-135 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harris et al (US 6,187,765) in view of Jakupovic et al (WO 96/32095) as applied to claims 65, 66, 68-83, 94-97, 101-109, 112, 115-117, 124-126, 130-132 and 139-141 above, and further in view of Morice et al (Clin. Pharmacol. Ther., 1996).

Harris and Jakupovic teach as set forth above. The references do not teach the treatment of COPD.

Morice teaches the administration of nebulized budesonide for the treatment of COPD. See abstract.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare a sterile suspension comprising micronized budesonide, as discussed above. It would be further obvious to administer this product for the treatment of COPD with a reasonable expectation of success because Morice had taught that budesonide has this utility.

Claims 148, 149, 152 and 153 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harris et al (US 6,187,765) in view of Jakupovic et al (WO 96/32095) as applied to claims 65, 66, 68-83, 94-97, 101-109, 112, 115-117, 124-126, 130-132 and 139-141 above, and further in view of Jonsson et al (Drug Metab. Dep., 1995).

Harris and Jakupovic teach as set forth above. The references are silent regarding the isomeric form.

Jonsson teaches that the 22R epimer has three times the anti-inflammatory potency as the 22S epimer.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare a sterile suspension comprising micronized budesonide, as discussed above. It would be further obvious to prepare such a suspension using the 22R epimer because of the greater anti-inflammatory potency. One of ordinary skill would reasonably expect success in preparing such a suspension.

LCM Claims 84-93, 98-100, 146 and 147 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jakupovic et al (WO 96/32095) in view of Harris et al (US 6,187,765) and Tainsh et al (WO 95/31964).

Jakupovic teaches as set forth above. The reference does not teach a sterile product or the preparation of a suspension. In preparing this product under non-sterile conditions, it would inherently comprise viable microorganisms. Harris teaches that a suspension of budesonide is known and the importance of sterility for inhaled compositions.

Tainsh teaches the preparation of a suspension comprising the glucocorticosteroid, fluticasone. The reference further teaches the sterilization of the prepared suspension using steam. See paragraph bridging pages 4 and 5.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare particles of budesonide as prepared by Jakupovic for use in a suspension as described by Harris and sterilize this suspension by steam as described by Tainsh for human administration. In the absence of unexpected results, one of ordinary skill would reasonably expect success in using this sterilization process because it is taught for a sterilization of a suspension comprising a glucocorticosteroid. Although these claims are product-by-process, the burden is on Applicant to demonstrate a difference between the product prepared according to that described by the references and that prepared according the invention.

Claims 150, 151 and 154-157 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jakupovic et al (WO 96/32095) in view of Harris et al (US 6,187,765) and Tainsh et al (WO

95/31964) as applied to claims 84-93, 98, 146 and 147 above, and further in view of Jonsson et al (Drug Metab. Dep., 1995).

Jakupovic , Harris and Tainsh teach as set forth above. The references are silent regarding the isomeric form.

Jonsson teaches that the 22R epimer has three times the anti-inflammatory potency as the 22S epimer.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare a sterile suspension comprising micronized budesonide, as discussed above. It would be further obvious to prepare such a suspension using the 22R epimer because of the greater anti-inflammatory potency. One of ordinary skill would reasonably expect success in preparing such a suspension.

Double Patenting

Claims 65-70, 72-80, 84-117, 121-132, 136-144, 146 and 147 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,686,346 in view of Harris et al (US 6,187,765) and Tainsh et al (WO 95/31964).

Claims 1, 11, and 12 of '346 recite a suspension (or administration of said suspension) comprising budesonide suspended in an aqueous medium. The claims do not require that the suspension be sterile or recite all the various additives. The claims recite the treatment of mammals but no humans specifically.

Although it would be obvious to one of ordinary skill prepare a suspension for inhalation in sterile form, Harris teaches this explicitly. Tainsh teaches steam sterilization of a suspension of a glucocorticosteroid.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to sterilize the suspension because it is desirable for inhaled products to be sterile. One of ordinary skill would reasonably expect success in using the steam sterilization process as described by Tainsh. With regard to the various additives, one of ordinary skill would look to the written description, particularly the examples, which comprise micronized budesonide and the recited additives. It would be further obvious to treat humans with a reasonable expectation of success.

Claims 65-70, 72-80, 84-117, 121-132, 136-144, 146 and 147 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1, 3, 7 and 8 of U.S. Patent No. 6,291,445 in view of Harris et al (US 6,187,765) and Tainsh et al (WO 95/31964).

Claims 1, 3, 7 and 8 of '445 recite a suspension (or administration of said suspension) comprising budesonide suspended in an aqueous medium. The claims do not require that the suspension be sterile or recite all the various additives. The claims recite the treatment of mammals but no humans specifically.

Although it would be obvious to one of ordinary skill prepare a suspension for inhalation in sterile form, Harris teaches this explicitly. Tainsh teaches steam sterilization of a suspension of a glucocorticosteroid.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to sterilize the suspension because it is desirable for inhaled products to be sterile. One of ordinary skill would reasonably expect success in using the steam sterilization process as described by Tainsh. With regard to the various additives, one of ordinary skill would look to the written description, particularly the examples, which comprise micronized budesonide and the recited additives. It would be further obvious to treat humans with a reasonable expectation of success.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Monday, Tuesday and Thursday from 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Anna Jiang (571) 272-0627, may be contacted. The fax number for Group 1600, Art Unit 1623 is (703) 872-9306.

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Leigh C. Maier

Leigh C. Maier
Primary Examiner
April 27, 2007